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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/577,409 | 04/25/2006 | Oreste Piccolo | 207,561 | 1407 |

7590 01/04/2011

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| EXAMINER | |
|---|---|
| SCHLIENTZ, NATHAN W | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1616 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 01/04/2011 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/577,409 | PICCOLO ET AL. | |
| | Examiner | Art Unit | |
| | Nathan W. Schlientz | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-28* is/are pending in the application.

4a) Of the above claim(s) *25-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

Claims 16-28 are pending in the present application. Claims 25-28 are withdrawn as being directed to a nonelected invention. Therefore, claims 16-24 are examined herein on the merits for patentability. No claim is allowed at this time.

### *Claim Interpretation*

With regard to claim 16 and the recitation, "both components (i) and (ii) are jointly complexed with cyclodextrin". The instant specification states on page 5, lines 19-23, "The joint complexing of insecticide and/or growth regulator and synergistic compound with cyclodextrin has surprisingly resulted in a significant increase in the effectiveness of the composition compared with a mixture of the two components complexed individually." Therefore, claim 16 is construed to mean that components (i) and (ii) are complexed with the same cyclodextrin to form a (i)/(ii)/CD complex, but does not include mixtures of component (i) complexed with cyclodextrin and component (ii) complexed with cyclodextrin (i.e., a (i)/CD complex mixed with a (ii)/CD complex).

### *Withdrawn Rejections*

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or

newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 16-18, 20, 21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Mifune et al. (US 3,846,551).

Mifune et al. disclose compositions comprising a pyrethroid with a cyclodextrin which contributes to the improvement of the stability of the pyrethroids to heat and light and exhibits insecticidal and acaricidal effects (col. 1, ln. 4-10). Mifune et al. further disclose that the cyclodextrins available are α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin (col. 3, ln. 52-59). Mifune et al. disclose that the active ingredient can be formed by contacting at least one pyrethroid intimately with at least one cyclodextrin in the presence of water, it will be readily understood that depending upon the formulation, the interacted product can be formed at the time of preparing the final pesticidal composition instead of preparing the interacted product in advance and then blending it with a diluent or carrier. For instance, in the case of a wettable powder, the interacted product can be formed during its preparation (col. 5, ln. 27-37).

The insecticidal and acaricidal composition of Mifune et al. may be in various formulations, such as a liquid, emulsifiable concentrate, wettable powder, oil, aerosol, paste, fumigant, dust, granule, tablet, or pellet (col. 5, ln. 38-41). The insecticidal and acaricidal composition contains various gaseous, liquid or solid diluents or carriers, and if desired, may be further contain various assistants, such as a surface active agent, emulsifier, dispersing agent, spreader, sticker, synergist, antioxidant, ultraviolet absorbent, and other insecticide (col. 5, ln. 43-49), wherein examples of the synergist include piperonyl butoxide (col. 6, ln. 32).

Mifune et al. further disclose examples wherein a pyrethroid, cyclodextrin and piperonyl butoxide are well kneaded to form a paste (Formulation Example 7). Cyclodextrin complexes are known to form by kneading with other components, such as pyrethroids and synergists (col. 4, ln. 1-19). The proportions of the pyrethroid to the cyclodextrin in the resulting complex may vary over a range of 0.5 to 1.5 mols per mol of the cyclodextrin (col. 4, ln. 26-29). Therefore, the compositions according to Formulation Example 7 would comprise both the pyrethroid and the synergist complexed with cyclodextrin since they were well kneaded in the presence of cyclodextrin in water.

*Response to Arguments*

Applicant argues that Mifune et al. describe the complexation between the insecticide and a cyclodextrin, but nowhere is joint complexation also with a synergistic compound disclosed. Mifune et al. states that the preformed interacted compound of insecticide and beta-cyclodextrin is mixed with PBO, stearic acid and Tween 60. The

complex therefore which is already formed is made by the insecticide and the cyclodextrin.

However, the examiner respectfully argues that Mifune et al. disclose mixing an interacted compound of furamethrin and β-cyclodextrin, PBO, stearic acid, SPAN 60, Tween 60, and water, wherein the mixture is well kneaded (Formulation Example 7). Mifune et al. disclose sufficiently kneading the active with cyclodextrin and water in a kneader to prepare a cyclodextrin complex (col. 4, ln. 1-19). Therefore, it is the position of the examiner that kneading a mixture of an interacted compound of furamethrin and β-cyclodextrin with PBO in water will result in jointly complexing both the furamethrin and PBO with the CD.

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP 716.01(c)(II). Therefore, absent evidence to the contrary, the examiner respectfully argues that Mifune et al. disclose jointly complexing both furamethrin and PBO with CD.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 16-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mifune et al. (US 3,846,551) and Szejtli et al. (US 4,524,068).

*Determination of the scope and content of the prior art*

(MPEP 2141.01)

Biebel et al. teach that pyrethrum extract is an ideal pesticide, but it has low light stability (Abstract; and pg. 175, Introduction). This drawback can be overcome by the complexation of pyrethrum extract with γ-cyclodextrin (Abstract; pg. 176, sentence bridging the left and right columns; and section 2.2.1). Biebel et al. further teach that pyrethrins, such as pyrethrum extract, experience rapid metabolism which is a drawback concerning the frequency of application. Therefore, synergists are added to ensure an insecticidal effect or pyrethrum, wherein the most widely used synergist in the

last decades has been piperonyl butoxide (PBO) (pg. 175, right column, ln. 2-12). Biebel et al. teach that synergists may also profit from a complexation with cyclodextrins, and thus sesamol was also complexed with γ-cyclodextrin (pg. 176, right column, ln. 2-7; and section 2.2.2). Biebel et al. teach compositions comprising a 10 to 50 fold excess synergist compared to pyrethrum (Table 1).

Szejtli et al. teach that numerous efficient insecticidal active ingredients are decomposed by the mitochondrial non-specific oxidative enzymes of the insects so rapidly that the exerted effect is very low. The synergistic effect of piperonyl butoxide and other similar synergistic components manifests itself in the fact that the said agent inhibits the rapid inactivation of the active ingredient by the oxidase enzymes of mixed function. The said synergistic agents are useful not only in combination with insecticides but also with fungicides and they are capable of increasing the effect of the active ingredient by ten to fifty times (col. 1, ln. 15-25).

Szejtli et al. teach that piperonyl butoxide is generally used to synergize pyrethrins and synthetic pyrethroids and organic phosphate compositions. Studies relating to the relationship between the synergistic effect and chemical structure of piperonyl butoxide (referred to furtheron as "PBO") have shown that the methylenedioxy phenyl group is the most important functional moiety of the molecule and that any modification or change of the said group leads to the complete loss or strong reduction of the synergistic activity (col. 1, ln. 34-43).

Szejtli et al. further teach that it is known that the active ingredients of drugs and pesticides can be included into cyclodextrins and the inclusion complexes thus obtained

can influence and modify the biological characteristics thereof. It has been found that the solubility of piperonyl butoxide (PBO) and other similar synergistic agents can be increased by forming a cyclodextrin complex. The inclusion complex goes into solution more rapidly and thereby the velocity of penetration through the biological membrane is increased as well. The absolute activity of the synergistic component becomes higher and therefore in an identical active ingredient concentration the biological effect is exhibited more promptly and stronger or the same biological effect can be reached by using a lower active ingredient concentration (col. 1, ln. 59 through col. 2, ln. 6).

Szejtli et al. teach that the advantages of the piperonyl butoxide-cyclodextrin inclusion complex over the piperonyl butoxide molecule can be summarized as follows: (1) the inclusion complexes are solid crystalline products, which can be easily handled and readily formulated; (2) the amount of piperonyl butoxide which can be dissolved from the inclusion complex is by 2.5 to 4 times larger than the amount of pure piperonyl butoxide dissolved in aqueous solution; (3) as a result of the higher water solubility the absorption of the synergistic agent is increased and the velocity of penetration through the biological membrane becomes larger and consequently the absolute concentration of the active ingredient increases as well; and (4) as a consequence of the aforesaid when using identical active ingredient concentration the biological effect is quicker and stronger and an identical active biological effect can be achieved with the aid of a lower active ingredient concentration (col. 2, ln. 30-49).

The piperonyl butoxide-cyclodextrin inclusion complex can replace the original synergistic agent in insecticidal or fungicidal combinations to synergize the activity of pyrethrins, synthetic pyrethroids or organophosphates (col. 2, ln. 50-55).

*Ascertainment of the difference between the prior art and the claims*

*(MPEP 2141.02)*

Biebel et al. and Szejtli et al. do not explicitly disclose jointly complexing the pyrethrin or pyrethroid and the synergist with cyclodextrin, as instantly claimed. However, Biebel et al. teach complexation of pyrethrum extract with γ-cyclodextrin, and also teach that synergists may also profit from a complexation with cyclodextrins. Szejtli et al. teach that it is known that the active ingredients of drugs and pesticides can be included into cyclodextrins and the inclusion complexes thus obtained can influence and modify the biological characteristics thereof. It has been found that the solubility of piperonyl butoxide (PBO) and other similar synergistic agents can be increased by forming a cyclodextrin complex. The inclusion complex goes into solution more rapidly and thereby the velocity of penetration through the biological membrane is increased as well. The absolute activity of the synergistic component becomes higher and therefore in an identical active ingredient concentration the biological effect is exhibited more promptly and stronger or the same biological effect can be reached by using a lower active ingredient concentration. Therefore, Biebel et al. and Szejtli et al. clearly teach the benefits of forming inclusion complexes of pyrethrins or pyrethroids in cyclodextrin, as well as the benefits of forming inclusion complexes of synergists such as PBO in cyclodextrin.

*Finding of prima facie obviousness*

*Rational and Motivation (MPEP 2142-43)*

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of the invention to form an inclusion complex of both pyrethrins or pyrethroids and synergist in a cyclodextrin, with the reasonable expectation that inclusion of the pyrethrin or pyrethroid will increase its bioefficacy, and inclusion of the synergist will increase its solubility as well as synergistically increasing the bioefficacy of the pyrethrin or pyrethroid.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

*Response to Arguments*

Applicant argues that complexes with many insecticides (pyrethroids) prepared in accordance with the claimed invention are always much more efficient as reported in the specification and exemplified in biological assays in comparison with all the commercial products, even when the concentration of both components, insecticide (pyrethroid) and synergist, is lower than the optimal concentration found in Biebel et al. In addition, the claimed complexes have been found to be more active than the mixtures of the two agents. Applicant further submitted Annex 1 for the examiner's consideration.

The examiner respectfully argues that the samples prepared and the data obtained by the mortality assay shown in Example 4 of the instant specification is insufficient to show that the study is a true side by side comparison. The Example does not teach how the formulations were prepared or the exact components of each formulation; the actual data obtained from the mortality assay is not present for direct comparison; and there is not a comparison with the mixture of cypermethrin and PBO without cyclodextrin. With regard to the other mortality assays disclosed in the instant specification (Examples 18-20), there were no comparisons of the pyrethroid complexed with cyclodextrin, or pyrethroid and PBO separately complexed with cyclodextrin. Also, it is noted that the data in Example 20, Table 3, appears to be incorrect. The number of insects alive per number of total insects indicates survival rate (i.e., 6/10 indicates a survival of 60% and a mortality of 40%). With regard to Annex 1, the examples do not compare formulations according to the instant invention with a mixture of pyrethroid and PBO separately complexed with CD. It is not clear that the increase in mortality in Examples 21-23 is not merely additive as opposed to synergistic since there is no comparison wherein the pyrethroid and PBO are separately complexed with CD. Examples 22 and 23 don't even show data for the pyrethroid mixed with a synergist, which is well known to increase the efficacy and thus increase the mortality. It is also well known in the art that complexing with CD increases the efficacy, and thus it is expected that complexing with CD will result in a higher mortality. Also, the data is not commensurate in scope with the claims. Claim 16 is drawn to (1) any pyrethroid or a component with insect growth regulator activity and (2) any synergist, at any ratio of

active(1)/synergist(2)/CD, whereas the examples only show combinations of pyrethroids with PBO at narrow ratios.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### *Contact Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is (571)272-9924. The examiner can normally be reached on 9:00 AM to 5:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NWS

/John Pak/
Primary Examiner, Art Unit 1616